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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	13

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
500,135	ESTELL et al
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 6/18/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-3, 5, 7-14, 16-28 is/are pending in the application.

Of the above claim(s) 3, 11-13, 16-28 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-2, 5, 7-10, 14 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4, 5

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ ~~Other~~ RAW SEQUENCE LISTING - ERROR REPORT

Office Action Summary

The response filed on 6/18/01 (Paper 10) has been received. Claims 1-3, 5, 7-14 and 16-28 are pending.

Applicant's election without traverse of Group I (claims 1-2, 5 and 7-14) in Paper No. 10 is acknowledged.

Applicant has indicated that "subgroup A" of Group I is elected. This statement is unclear, since the restriction requirement did not indicate subgroups. The examiner notes, however that claim 1 is being examined for the embodiment in which the immunogenic response is lessened, in accord with the restriction requirement's defining of the groups.

Claims 3, 11-13 and 16-28 are withdrawn from consideration.

The disclosure is objected to because of the following informalities: at page 22, the "R factor" is not defined by any formula.

Appropriate correction is required.

In example 1, numerous exponent values have not been indicated as exponents.

Since the parent application was incorporated by reference in its entirety, applicant may correct the above defects according to what is recited in the parent.

The CRF filed on 6/18/01 contains errors. See attached report.

Claims 1-2, 5, 7-10 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not given an adequate description of what is meant by a "different immunogenic response" (as in claim 1) or even such a response interpreted as "less" (as in claim 2).

Applicant has only described polypeptides (enzymes) which give less of an immunogenic response, as assessed in terms of a T-cell proliferative response against enzymes for which one wishes to obtain a less allergenic product. Applicant has not described, for example, how one might identify and alter t-cell epitopes such that other kinds of immunogenic responses could be lessened – e.g. induction of tolerance to endogenous enzymes which serve as autoantigens in an autoimmune disease. The genus of enzyme variants which would produce such altered

immunogenic responses (including a wide variety of different kinds of responses) includes a large and diverse group of structural variants, and there is no disclosure of the distinguishing attributes shared by members of the genus. Structural features that would distinguish the altered epitopes from other epitopes have not been disclosed.

Claims 1-2, 5, 7-10 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for providing enzyme variants which produce a lessened allergenic response, does not reasonably provide enablement for providing enzyme variants which produce an altered or lessened immunogenic response of any and all types. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. As noted supra with respect to the description requirement , applicant's disclosure is limited to showing one how to alter enzymes such that their T-cell epitopes would be altered to produce a lessened allergenic response. Not direction has been given as to how to provide altered products which would alter other kinds of immunogenic responses (e.g. to autoantigens involved in an autoimmune disease).

Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's disclosure has not adequately described what are sequences from homologues to the protease of interest that are sequences which produce an altered or lesser immunogenic or allergenic response.

Applicant has not identified what are such homologues in terms of structure which would differentiate them from homologues which produce an allergenic response. The sequences of homologues which might produce a lessened allergenic response would include a large and diverse group of structural variants. There is no disclosure of the distinguishing attributes (even highly homologous sequences could still induce T-cell responses if they retain a motif which is recognized by MHC and T-cell receptors) of the genus. Structural features that would distinguish the sequences of the genus from other homologous sequences have not been disclosed. Mere statements of a desired goal or a disclosure of how one might find such do not constitute a description of the genus of desired homologues per se.

Prior to examination of the claims over the prior art. The effective filing date of the claims must by established.

It is noted that the enzyme Markush group of claim 1 was not disclosed in parent 09/060,872.

The notion of "a different immunogenic response", as opposed to a lessened immunogenic response, was not disclosed in 09/060,872.

The concepts of claims 8-10 were not disclosed in 09/060,872.

For all of the above reasons the claims are only granted benefit of the instant filing date of 2/8/00.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5 and 7 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over King (US 5,593,877).

Prior to stating the teachings of the reference the examiner notes that instant claim 1 states (line 4) "said polypeptide of interest comprises a T-cell epitope". Hence, it is considered proper to reject the claims over any reference showing a peptide/polypeptide segment corresponding to a T-cell epitope.

King teaches identification of T-cell epitopic sites in phospholipase or hyaluronidase allergens found in insect venom. See col. 22, lines 23-44. Immunomodulatory peptides containing the identified T-cell epitopes can be therapeutically administered to patient. See col. 22, lines 7-13 and 29-40. See col. 19, line 33-col. 20, line 57 for teachings of how to identify immunomodulatory peptides. The peptides can be modified by amino acid substitutions (col, 18, lines 10-31) or by chemical treatments (col. 19, lines 5-19). Peptides that induce T-cell Anergy can be identified (col. 20, lines 38-44).

Anticipation is stated on the basis that all that is required to arrive at applicant's polypeptide is taught within the four corners of the reference. Obviousness is stated in case it would be considered necessary to combine suggestions from various parts of the reference in order to provided a modified T-cell epitopic polypeptide having anergenic properties.

Claims 1-2, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Bott et al (EP 0,251,446) or (US 5,801,038).

Bott et al. disclose (Table II, col. 15) that substitution of tyr 171 with glutamine provides an expected useful mutation in subtilin from B. amyloliqueofaciens. This change corresponds to the instant embodiment (as disclosed at instant page 30, and in the parent application in claim 1) involving Y171Q.

This rejection is made on the basis that the substituted subtilisin of Bott et al. would inherently less allergenic that the native form of the enzyme, based upon applicant's own teachings. Even though the substitution taught by Bott et al. may not have been arrived at in the

same manner or for the purpose as instantly; a product is a product no matter what process it was made by.

Claims 1-2, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Seikstra (WO 96/34946 or US 5,837,517).

Seikstra et al. disclose (col. 15, line 23) various substituted subtilisins including those having the single substitution Y171Q, as disclosed in parent application claim 1.

For the sake of convenience, the above prior art rejections have referred only to the US references by column and line number. The corresponding EP and WO publications have not been provided, due to their large size. Upon request, the examiner will fax copies of relevant pages to applicant's representative.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 5, 7-9, and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15-22 of copending Application No. 09/255,501. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the claims encompass common subject matter for reasons explained in the paragraph further below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims encompass the subject matter of the copending claims limited to a modified, less allergenic protease in a svap or contact lens cleaning composition. It is noted that, in the disclosure of both the '501 and the instant applications, the exemplified embodiment is that a modified subilitisin having identical substitutions.

Instant claims 8-9, though not corresponding in their recitations to the claims of the '501 application are considered to encompass what is recited in copending claim 15, part (b) (I) or claim 17 part (b).

Claims 1-2, 5, 7-9 and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5, 24, 27 and 30 of copending Application No. 09/060,854. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims, though broader, would encompass the particular subtilisin and detergent composition claims in copending claims 5, 24, 27, and 30 of the '854 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders Ph.D. whose telephone number is (703) 308-3976. The examiner can normally be reached on M-F from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Saunders:mv

September 6, 2001

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644